

Appl. No. : 09/272,835
Filed : March 19, 1999

Sequence Rule Compliance

Along with the present Amendment, Applicants file a substitute Sequence Listing in paper copy and computer readable form along with a statement that the two versions are the same, and do not add new matter to the specification. The entry of the Sequence Listing, which is in full compliance with the requirement of 37 C.F.R. § 1.821 through 1.825, is respectfully requested. A copy of the "Notice to Comply" is returned with the present Amendment. The specific issues raised by the Examiner are addressed as follows.

(1) The Examiner noted that under 37 CFR 1.821 (a)(20(c-d)) "each sequence disclosed must appear separately in the 'Sequence Listing' and in the text of the description and claims (i.e., where first mentioned in the specification)," and suggested that the present application does not comply with the requirement. The current amendments to the specification are believed to overcome the present objection.

(2) The Examiner noted that "it remains unknown whether SEQ ID NOs: 18 or 20 represent murine, rat or human sequences." The Applicants respectfully disagree.

Applicants submit that it is clear from Figure 3 that SEQ ID NO: 18 is the sequence of *human* GFR α 3. Since Figure 3 was part of the application as originally filed, this information does not add new matter. SEQ ID NO: 20 is clearly described on page 56, line 6-7, as including *murine* GFR α 3 sequence. This information is also clearly reflected in the Substitute Sequence Listing submitted herewith.

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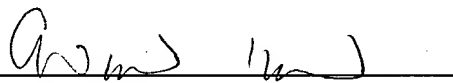
Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned "Version with markings to show changes made."

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: November 8, 2001

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Version with markings to show changes made

In the Specification:

Please replace the paragraph beginning at page 3, line 16, with the following rewritten paragraph:

--In one embodiment, the invention provides an isolated nucleic acid molecule having at least about 65% sequence identity to (a) a nucleic acid sequence encoding a GFR α 3 polypeptide comprising the sequence of amino acids 27 to 400 of SEQ ID NO: 15, amino acids 27 to 369 of SEQ ID NO: 17 or amino acids 27 to 374 of SEQ ID NO: 5 or (b) the complement of the nucleic acid molecules of (a). In another embodiment, the nucleic molecule sequence above comprises a ligand-binding domain of a GFR α 3 polypeptide of amino acids 85 to 360 of SEQ ID NO: 15, amino acids 84 to 329 of SEQ ID NO: 17, or the sequence of amino acids 110 to 386 of SEQ ID NO: 20, or their complementary nucleic acids. The isolated nucleic acid comprises a GFR α 3 encoding sequence which preferably hybridizes under stringent conditions to nucleic acid sequences encoding a GFR α 3 polypeptide of the invention. The sequence identity preferably is at least about 75%, more preferably at least 85%, even more preferably at least 90%, most preferably at least 95%. In one aspect, the encoded polypeptide has at least about 75%, preferably at least 80%, more preferably at least 85%, even more preferably at least 90%, and most preferably at least about 95% sequence identity with a polypeptide having amino acid residues 27 to 400 of SEQ ID NO: 15, amino acids 27 to 369 of SEQ ID NO: 17, amino acids 27 to 374 of SEQ ID NO: 5, a ligand-binding domain of a GFR α 3 polypeptide of amino acids 84 to 360 of SEQ ID NO: 15, amino acids 84 to 329 of SEQ ID NO: 17, or the sequence of amino acids 110 to 386 of SEQ ID NO: 20. Preferably the identity is to amino acid residues 27 to 400 of SEQ ID NO: 15 and DNA encoding it. In a further embodiment, the isolated nucleic acid molecule comprises DNA encoding a GFR α 3 polypeptide having amino acid residues 27 to 400 of SEQ ID NO: 15, or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the invention provides a nucleic acid of the full length protein of clone DNA48613 (SEQ ID NO: 14), DNA48614 (SEQ ID NO: 16) or murine GFR α 3 (SEQ ID NO: 4) (clone 13). [,]DNA48613-1268 (SEQ ID NO: 14) and DNA48614-1268 (SEQ ID NO: 16) were deposited with the ATCC under accession numbers ATCC 209752 (Designation: DNA48613-

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1268)[,]and ATCC209751 (Designation: DNA48614-1268), [and ATCC _____,
]respectively, on April 07, 1998.--

Please replace the paragraph beginning at page 7, line 23, with the following rewritten paragraph:

--Figures 1A-B shows the nucleotide sequence (SEQ ID NO: 4) and deduced amino acid sequence (SEQ ID NO: 5) of a native sequence of murine GFR α 3.--

Please replace the paragraph beginning at page 7, line 30, with the following rewritten paragraph:

--Figure 3 shows the alignment comparison between murine (SEQ ID NO: 5) and human (SEQ ID NO: 15) GFR α 3 amino acid sequences. Conserved residues are boxed.--

Please replace the paragraph beginning at page 7, line 32, with the following rewritten paragraph:

--Figure 4 shows the alignment comparison between human GFR α 3 (SEQ ID NO: 15) (from DNA48613) and its splice variant (SEQ ID NO: 17) (from DNA48614). Conserved sequences are boxed. The 30 amino acid deletion sequence is indicated.--

The paragraph beginning at page 19, line 16, has been amended as follows:

--The variants can be those encoded by an isolated nucleic acid molecule having at least about 65% sequence identity to (a) a nucleic acid sequence encoding a GFR α 3 polypeptide comprising the sequence of amino acids 27 to 400 of SEQ ID NO: 15, amino acids 27 to 369 of SEQ ID NO: 17 or amino acids 27 to 374 of SEQ ID NO: 5 or (b) the complement of the nucleic acid molecules of (a). Further, the variants can be encoded by nucleic molecule sequences comprising a ligand-binding domain of a GFR α 3 polypeptide of amino acids 84 to 360 of SEQ ID NO: 15, amino acids 84 to 329 of SEQ ID NO: 17, or the sequence of amino acids 110 to 386 of SEQ ID NO: 20, or their complementary nucleic acids. These isolated nucleic acid molecules preferably comprise a GFR α 3 encoding sequence which preferably hybridizes under stringent conditions to nucleic acid sequences encoding a GFR α 3 polypeptide of the invention. The sequence identity preferably is 75%, more preferably at least 85%, even more preferably at least

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90%, most preferably at least 95%. Typically, the polypeptide has at least about 75%, preferably at least 80%, more preferably at least 85%, even more preferably at least 90%, and most preferably at least about 95% sequence identity with a polypeptide having amino acid residues 27 to 400 of SEQ ID NO: 15, amino acids 27 to 369 of SEQ ID NO: 17, amino acids 27 to 374 of SEQ ID NO: 5, a ligand-binding domain of a GFR α 3 polypeptide of amino acids 84 to 360 of SEQ ID NO: 15, amino acids 84 to 329 of SEQ ID NO: 17, or the sequence of amino acids 110 to 386 of SEQ ID NO: 20. Preferably the identity is to amino acid residues 27 to 400 of SEQ ID NO: 15 and DNA encoding it. The isolated nucleic acid molecule can contain a DNA encoding a GFR α 3 polypeptide having amino acid residues 27 to 400 of SEQ ID NO: 15, or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The protein can be encoded by the nucleic acid encoding the full length protein of clone DNA48613 (SEQ ID NO: 14), DNA48614 (SEQ ID NO: 16) or murine GFR α 3 (SEQ ID NO: 4) (clone 13); or one that hybridizes thereto under stringent conditions. [,]DNA48613 (SEQ ID NO: 14) and DNA48614 (SEQ ID NO: 16) were deposited with the ATCC under accession numbers ATCC 209752 (Designation: DNA48613-1268)[,] and ATCC 209751 (Designation: DNA48614-1268), [and ATCC _____,]respectively, on April 07, 1998[, or one that hybridizes thereto under stringent conditions].--

The paragraph beginning at page 49, line 9, has been amended as follows:

--The deduced amino acid sequence (SEQ ID NO: 17) of DNA48614 and comparison to SEQ ID NO: 15, revealed it to be an alternatively spliced form of DNA48613, with a 30 amino acid deletion (amino acid positions 127-157, counting from the initiation methionine), as shown in Figure 4. Interestingly, none of the cysteines are deleted in this clone. Clones DNA48613[,]
and DNA48614[and mGFR α 3(clone 13) variant] have been deposited with ATCC and are assigned ATCC deposit nos. 209752 (Designation: DNA48613-1268)[,]and 209751 (Designation: DNA48614-1268), [and _____,]respectively.--

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The paragraph beginning at page 58, line 36, has been amended as follows:

| -- | <u>Material</u> | <u>ATCC Dep. No.</u> | <u>Deposit Date</u> |
|----|---------------------------|----------------------|---------------------|
| [| mGFR α 3(clone 13) | _____ | _____] |
| | DNA48613 | 209752 | April 07, 1998 |
| | DNA48614 | 209751 | April 07, 1998-- |

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